Claims 39, 42-52, 57, 60-65, 68, 74, 76-82 and 88 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Furie et al. (EP 0496832). This ground of rejection is respectfully traversed.

Furie et al. relates to a method for inhibiting the binding of cells, such as platelets, bearing P-selectin and a P-selectin ligand through the use of agents such as carbohydrates and antibodies to P-selectin. The reference also recites that this method is useful for treating biological conditions including atherosclerosis, clotting and inflammation.

However, Furie et al. does not disclose that P-selectin antibodies can be used to inhibit the interaction of both P-selectin, and E-selectin and a ligand of E-selectin, or L-selectin and a ligand of L-selectin as required by the present claims. In fact, there is no mention in Furie et al. of E-selectin, ELAM-1, or L-selectin, and consequently, there is no indication from the reference that the antibodies described therein would inhibit E-selectin and a ligand of E-selectin, or L-selectin and a ligand of L-selectin. Applicants direct the Examiner's attention to the previously submitted declaration regarding the significance of this characteristic.

Claims 39-52, 57, 60-68, 71-74, 80-82, 94, 86 and 88 have been rejected under 35 U.S.C. 102(b) as being anticipated by Palabrica et al. (WO 93/06863). This ground of rejection is traversed.

Palabrica et al. relates to the use of P-selectin antibodies to inhibit vascular narrowing associated with post-angioplasty restenosis. Palabrica et al. is concerned with the therapeutic use of P-selectin antibodies following a surgical procedure, and there is no disclosure in the reference regarding the use of P-selectin antibodies to prevent or inhibit atherosclerosis as presently claimed by applicants. Moreover, there is also no disclosure in the reference that operable antibodies should be capable of inhibiting both P-selectin and E-selectin or L-selectin binding with their respective ligands.

Claims 39-52, 57, 60-65, 68, 73-74, 80-82, 85, 86 and 88 have been rejected under 35 UI.S.C. 102(a)(e) as being anticipated by McEver et al. This ground of rejection is also traversed.

McEver et al. describe a method for modulating an inflammatory response in a patient by treating the patient with inhibitors for GMP-140, such as GMP-140 antibodies. The inflammatory responses described in the reference include circulatory shock, organ transplant rejection, myocardial infarction and acute respiratory distress syndrome. Atherosclerosis is not an inflammatory condition as that term is used in the McEver et al. reference.

Further, there is no indication from the McEver et al. reference that GMP-140 antibodies would also be useful to prevent the binding of E-selectin to a ligand of E-selectin, or L-selectin to a ligand of L-slectin, as required in the present claims. In fact, McEver et al. draws a distinction between GMP-140 and ELAM-1 as shown in col. 17 of the reference.

Claims 39-52, 57, 60-68, 71-74, 76-82, 84-85, 86 and 88 stand rejected under 35 U.S.C. 103(a) as obvious over the combination of Furie et al., and/or Palabrica et al., and/or McEver et al., in view of the known combination therapies used in the treatment of atherosclerosis as taught by Coller et al. (U.S.Patent No. 5,976,532). This ground of rejection is traversed.

The Furie et al., Palabrica et al. and McEever et al. references have been discussed previously. These references, either singly or in combination, fail to teach or suggest the methods and therapeutic agents of the present invention since the references do not disclose P-selectin antibodies which are effective for inhibiting both P-selectin and E-selectin or L-selectin binding with their respective ligands. These deficiencies are not cured by the Coller et al. reference which has been cited only for its disclosure of the use of combination therapies and vessel corrective techniques.

Applicants specification does not contain an admission that any aspect of the presently claimed invention is known in the art. The statement on pages 12-16 of the specification regarding administration of the therapeutic agent is part of the description of the methods for using the invention, and is not an acknowledgement that the present invention has been used in this manner by others.

In view of the foregoing facts and reasons, the present application is now believed to overcome the remaining rejections, and to be in proper condition for allowance. Accordingly, reconsideration and withdrawal of the rejections, and favorable action on this application, is solicited. The Examiner is invited to contact the undersigned at the telephone number listed below to discuss the status of this application.

Respectfully submitted,

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MARKED-UP SPECIFICATION

METHODS FOR TREATING AND PREVENTING ATHEROSCLEROSIS USING ANTIBODIES TO P-SELECTIN

ABSTRACT

A method for treating or preventing atherosclerosis in a mammal is described. An [agent] antibody for inhibiting the interaction between P-selectin and a ligand of P-selectin and between E-selectin and a ligand of E-selectin is provided. The [agent] antibody is administered to a mammal in need of such treatment to cause this inhibition to occur.---

MARKED-UP CLAIMS

39. (Amended) A method for treating or inhibiting atherosclerosis in a mammal comprising:

providing [an agent] a P-selectin antibody for inhibiting an interaction between P-selectin and a ligand of P-selectin, and between E-selectin and a ligand of E-selectin; and

administering said [agent] antibody to a mammal in need of such treatment so as to cause such inhibition to occur [wherein said agent is selected from the group consisting of an inhibitory protein, an inhibitory peptide, an inhibitory carbohydrate, an inhibitory antibody, an inhibitory sulfatide, a substance obtained from a snake venom or a plant extract, and an inhibitor of granular release].

40. (Amended) The method of claim 39 wherein said [agent] antibody is administered to the mammal in conjunction with a vessel-corrective technique.

61. (Amended) The method of claim 39 wherein said [agent] antibody is an inhibitor of a molecule required for the synthesis, post-translational modification or functioning of said P-selectin or said ligand of P-selectin.

62. (Amended) The method of claim 39 wherein said [agent] antibody inhibits interaction between said P-selectin and said ligand of P-selectin or between E-selectin and said ligand of E-selectin so as to [at least partially] inhibit formation of an atherosclerotic streak, or [at least partially] reverse a formed atherosclerotic fatty streak.

63. (Amended) The method of claim 39 wherein said [agent] antibody inhibits interaction between said P-selectin and said ligand of P-selectin or between E-selectin and said ligand of E-selectin so as to [at least partially] inhibit formation of an atherosclerotic intermediate lesion, or [at least partially] reverse a formed atherosclerotic intermediate lesion.

64. (Amended) The method of claim 39 wherein said [agent] antibody inhibits interaction between said P-selectin and said ligand of P-selectin or between said E-selectin and said ligand

of E-selectin so as to [at least partially] inhibit formation of an atherosclerotic fibrous plaque, or [at least partially] reverse a formed atherosclerotic fibrous plaque.

65. (Amended) The method of claim 39 wherein said [agent] antibody inhibits interaction between said P-selectin and said ligand of P-selectin or between said E-selectin and said ligand of E-selectin so as to [at least partially] inhibit formation of an atherosclerotic lesion after a surgical procedure for [at least partially] inhibiting [restinosis] restenosis.

69. (Amended) A therapeutic agent in a dosage form and concentration suitable for treating or inhibiting atherosclerosis in a mammal in need of such treatment, said agent being effective to inhibit interaction between P-selectin and a ligand of P-selectin [or] and between E-selectin and a ligand of E-selectin, wherein said therapeutic agent is [selected from the group consisting of an inhibitory protein, an inhibitory peptide, an inhibitory carbohydrate, an inhibitory antibody, an inhibitory sulfatide, a substance obtained from a snake venom or a plant extract, and an inhibitor of granular release] a P-selectin antibody.

71. (Amended) The method of claim 39, wherein said [agent] antibody is administered at a dose of about 0.01 to about 200 mg/kg body weight.

72. (Amended) The method of claim [69] 39, wherein said [agent] antibody is administered at a dose of about 1 to about 100 mg/kg body weight.

73. (Amended) The method of claim 39, wherein said [agent] antibody further inhibits interaction between L-selectin and a ligand of L-selectin.

74. (Amended) A method for treating or inhibiting atherosclerosis in a mammal, comprising:

providing [an agent] a P-selectin antibody for inhibiting interaction between P-selectin and a ligand of P-selectin and between L-selectin and a ligand of L-selectin; and

administering said [agent] antibody to a mammal in need of such treatment so as to cause such inhibition to occur.

76. (Amended) The method of claim 39, wherein said [agent] antibody is administered in sequential exposures over a period of hours, days, weeks, months or years.

77. (Amended) The method of claim 39, wherein said [agent] antibody is administered repeatedly, or by controlled release delivery system.

78. (Amended) The method of claim 39, wherein the [agent] antibody is administered in combination with other therapeutic agents.

79. (Amended) The method of claim 39, wherein the [agent] antibody is administered as a pill, as an injection, or as an implant.